REMARKS

STATUS OF THE CLAIMS

Claims 8, 9, 12, 14-19, 23, 26, 28, 29, and 30 were pending in this application. Claim 30 has been amended. Following the amendments, claims 8, 9, 12, 14-19, 23, 26, 28, 29, and 30 will be pending and at issue.

SUPPORT FOR AMENDMENTS TO THE CLAIMS

Claim 30 has been amended to further clarify recitation of one embodiment of Applicant's invention, e.g., a method using attenuated PBMCs prepared as described in one example of the instant application. Support can be found throughout the specification as filed, e.g., page 8 and Example 1, pages 10 and 11.

The amendments to the claims therefore add no new matter and entry is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

Claim 30 was rejected under 35 U.S.C. § 112, first paragraph (a new matter rejection). The Examiner stated that:

> Again, Applicant has included some of the limitations found in the example but has excluded other. Specifically, the claim excludes cell culture expansion employing 50U/ml IL-2. In step d) a 10-14 day time period has been excluded. In step e) repeating steps c) and d) weekly has been excluded. Additionally, the limitation of step f) comprising the reduction of aberrant autoimmune T cells has not been found in the example.

Without agreeing with the Examiner's rejection but rather to further prosecution, Applicant has amended claim 30 to recite the noted limitations. Withdrawal of the rejection is requested.

Claims 8, 9, 12, 14-19, 23, 26, 28, and 30 were rejected under 35 U.S.C. 112, first paragraph (a new matter rejection). Applicant respectfully disagrees.

The Examiner reiterated the rejection from the prior office action and in response to Applicant's arguments stated that:

> Again, the specific limitations of the claims have not been found anywhere in the specification. While the specification may disclose vaccines comprising T cells; the method of making the vaccine comprising T cells recited in the claims employs PBMCs .

Without agreeing with the Examiner's rejection but rather to further prosecution, Applicant has additionally amended claim 30 to recite PBMCs. Page 10 of the specification describes using PBMCs and bovine total myelin proteins (last 2 lines). Withdrawal of the rejection as drawn to claim 30 is requested.

Turning to the remaining claims, Applicant reiterates the arguments from the response filed February 7, 2007 and incorporates those arguments by reference. At numerous points in the specification, including the claims as filed, Applicant used the terminology "T-cells" to describe the claimed invention, including methods of making the vaccine. For example, at page 8, lines 4-5, Applicant stated "Preferably, T-cells are removed from the patient by leukaphoresis." One of skill understands that "preferably" indicates that T-cells can be derived from PBMCs (e.g., are removed from the patient by leukaphoresis). "Preferably" does not indicate that the T-cells must be derived from PBMCs.

Further, what is conventional or well known to one skilled in the art need not be disclosed in detail. The fact that T-cells can be derived from a variety of sources including, e.g., PBMCs and CSF, is well-known to one of skill in the art and therefore did not need to be explicitly disclosed in the specification. In addition, one of skill in the art readily understands that the described method for making the vaccine can be modified to use non-PBMC sources of T-cells.

Applicant respects withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 8, 9, 12, 14-19, 23, 26, 28, and 30 were rejected under 35 U.S.C. 103(a) each as allegedly unpatentable over Stinissen et al. (1996) in view of Correale et al (1995) and the background teachings of the specification. Applicant respectfully disagrees.

The combination of art does not include each and every element of Claim 30

The combination of Stinissen and Correale does not render obvious Claim 30 because the combination of art does not include the element of "administering PBMCs." Stinissen teaches

administering cloned T-cells, not administering PBMCs. Correale does not remedy this deficiency; Correale also teaches cloning by limiting dilution and says nothing about administration.

In addition, amended Claim 30 recites "A method of treating secondary progressive multiple sclerosis in a human ..." Stinissen does not teach a method of treating secondary progressive MS. Instead, on page 506, Stinissen teaches that "In three vaccinated patients with chronic progressive MS, no obvious effects on the clinical course were seen." Applicant notes that the Examiner did not address this point in the Final Office Action.

The combination of art does not include each and every element of the remaining claims

Turning to claims 8, 9, 12, 14-19, 23, 26, and 28, Applicant reiterates arguments made in the prior Response regarding the failure of Stinissen and Correale to teach administration of T-cell lines, e.g., administration of non-cloned T-cells as taught by Applicant. Applicant believes that one of skill in the art after review of the application would understand that the invention does not encompass administration of isolated T-cell clones.

No expectation of success

In response to Applicant's arguments that one of skill in the art would have had no expectation of success when combining the clonal method taught by Stinissen with the additional MS myelin antigens taught by Correale (as supported by a subsequent publication by the same group that authored Stinissen, VAN DER AA (Van der AA et al (2003) T cell vaccination in multiple sclerosis patients with autologous CSF-derived activated T cells: results from a pilot study. Clin Exp Immunol 131:155-168)) the Examiner stated

> A review of the reference again discloses that the statement regarding the difficulty of generating T cell clones specific for three different myelin antigens is made in the Introduction section of the reference with no explanation. *Indeed, the next paragraph teaches that the authors were able to do that very thing, i.e., the generation of sufficient T cells for vaccination, with no particular difficulty*. Accordingly, the isolated statement regarding difficulty in generating T cell clones would not lead the skilled artisan to doubt the expectation of success with the claimed method... Additionally, Stinissen et al. did not teach any particular difficulty in establishing and expanding their T cell clones such that there would

have been a lack' of expectation of success.

Applicant respectfully points out that the Examiner has misread VAN DER AA. Nowhere does VAN DER AA teach generation of sufficient T-cells for vaccination using a clonal approach. Instead, VAN DER AA teaches administration of CSF-derived mononuclear cells that have not been through a clonal dilution. See VAN DER AA, page 157, first column, second paragraph ("Generation of CSF-derived activated CD4 T cell vaccines).

In conclusion, the combination of art does not include all elements of the claims and one of skill in the art would have no expectation of success when combining the cited art. Therefore, a prima facie case of obviousness is not made. Withdrawal of this ground of rejection of the claims is respectfully requested.

NEW REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The Examiner stated

> Claims 8, .9, 12, 14-19, 23, 26, and 28 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.
>
> The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the T cell lines of Claim 8.
>
> Applicant cites original pages 7 and 9-12 of the specification in support.
>
> A review of the cites reveals that T cell lines are disclosed only at page 12. Said disclosure is then only in the context of Example 1 and thus appropriate only for the method of Claim 30.

Applicant respectfully request clarification of the Examiner's rejection as T-cell lines are clearly described not just at page 12 but also at the additional cites recited in the earlier response:

- page 7, line 11; page 9, last paragraph (describing the composition of the invention to be a polyclonal set of T-cells "activated against epitopes" (plural) and inducing a response against "many different pathogenic T-cells.");
- page 10, line 21 ("To establish T-cell lines … ");

- page 11, line 3 ("T-cell lines were re-stimulated …"); and
- page 12, line 20 ("… were considered as responding T-cell lines.")

In addition, the last paragraph of page 9 and first paragraph of page 10 are clearly describing a T-cell vaccine that comprises T-cells lines, e.g., polyclonal T-cells (and not a mixture of more than one T-cell clones):

> Without wishing to be bound by any particular theory, the mechanism of action for the vaccine is believed to be a host response to the T-cell receptor(TCR) variable region on the irradiated pathogenic T-cell that comprises the vaccine. This region is the only area thought to be different on the pathogenic T-cell as compared to other naive or activated T-cells. The approach described herein is based on the hypothesis that there are many V□ and V□ families involved since progressive MS has so many different antigen specific responses and immunodominant epitopes may differ from patient to patient. This allows T-cells from each patient to be activated against epitopes it has seen in vivo. when inactivated by radiation, the TCRs become antigens and induce either an anti-idiotypic antibody or a T-cell response against the V□ and V□ regions of many different pathogenic T-cells in that patient. The result is either down regulation or killing of existing and future pathogenic responses. Since it is a "killed" vaccine, it may be necessary to give a booster once a year to perpetuate the anti-myelin specific T-cells inactivation or killing.

CONCLUSION

Withdrawal of the pending rejections and reconsideration of the claims are respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (415) 875-2316.

Respectfully submitted,
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